IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of	: Bentzien, J et al.	) Art Unit:	1626
U.S. Appln. No.	: 10/632,888	) Examiner:	Stockton, L.L.
Confirmation No.	: 3053		
U.S. Filing Date	: 08/01/2003		
Title of Invention	: Substituted Benzimidazole Compounds		
Attny. Docket No.	: 9/254		

Mail Stop Amendment
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DECLARATION OF HIDENORI TAKAHASHI, UNDER 37 CFR 1.132

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Hidenori Takahashi, solemnly states and declares as follows:

1. My technical background is as follows: I am a trained biochemist having received a Bachelor of Science degree in pharmacy from Tokyo University of Pharmacy in March 25, 1985 and a Ph.D. degree in pharmacy from the Tokyo University of Pharmacy in March 15, 1990.

I engaged in post doctoral studies in synthetic organic chemistry at the University of Pittsburgh, Department of Chemistry from September 1, 1994 to March 31, 1996,; I joined Boehringer Ingelheim Pharmaceuticals, Inc. as a Senior Scientist specializing in medicinal chemistry; and I presently hold the position of Principal Scientist.

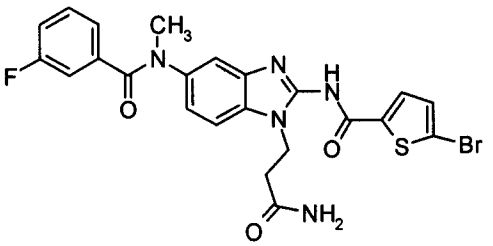
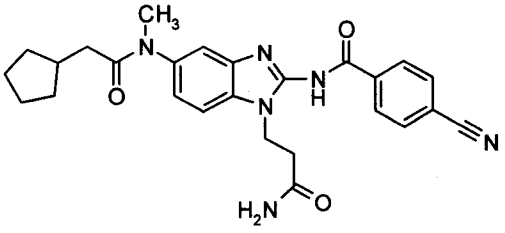
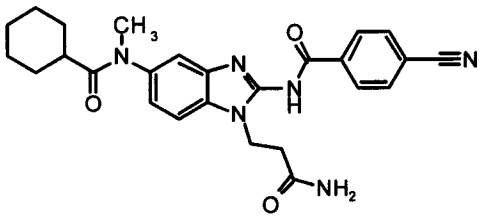
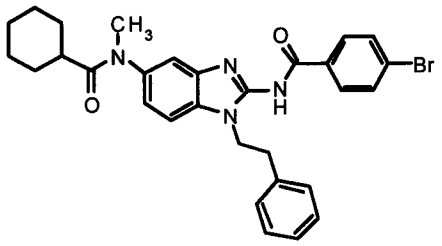
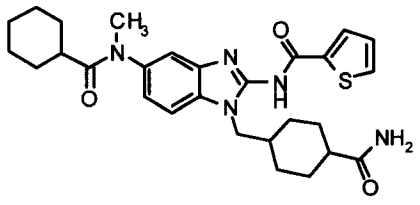
2. I am familiar with the subject matter of the above-noted patent application, and the Office Action dated 05/16/2005.

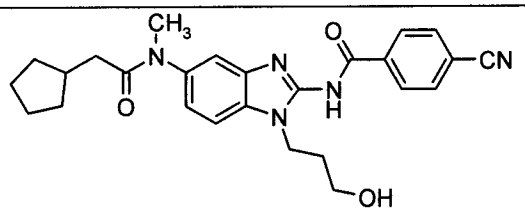
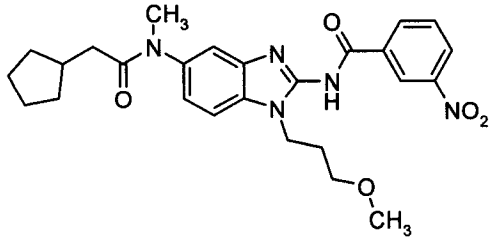
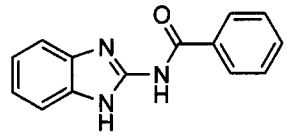
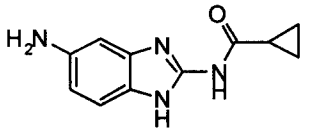
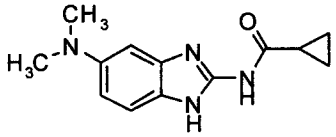
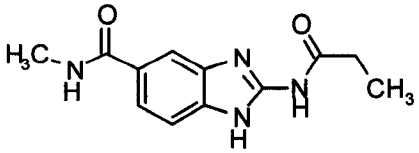
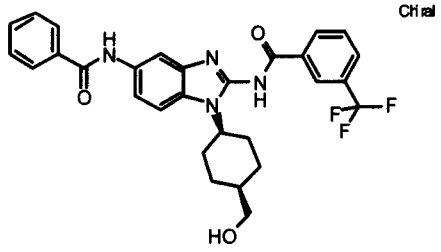
3. I am familiar with the cited prior art documents of Frenkel et al. (US 2003/0144286), Craig et al. (US 3,336,191), Craig et al. (US 3,401,171), and Smith Kline & French Labs (GB 1,122,957).

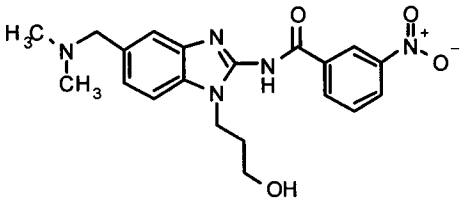
4. In my capacity of project leader I supervised the screening and evaluation of compounds under the research division's program directed to the development of compounds active against ITK.

5. In order to demonstrate the unexpectedly improved ITK inhibition activity for the compounds of the present invention, ITK assay found on page 143 of the present patent application was performed.

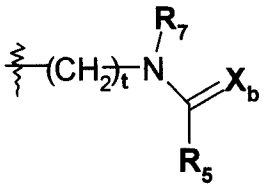
The compounds listed in the following table were screened using ITK assay found on page 143 of the present patent application. The results obtained are shown in the following table:

Compound	ITK IC_{50}(nM)
 (Third compound on page 36 of the above-noted patent application)	9
 (First compound on page 92 of the above-noted patent application)	23
 (Third compound on page 24 of the above-noted patent application)	15
 (Fourth compound on page 15 of the above-noted patent application)	36
 (Third compound on page 19 of the above-noted patent application)	9

 (Second compound page 62)	23
 (Last compound page 55)	190
 (US 3,336,191, example 18)	>= 13,000
 (GB1,122,957 example 22)	>= 14,000
 (US 3,401,171 example 22, US 3,336,191 example 30)	>= 12,000
 (US 3,401,171, column 3, lines 8-9)	>= 12,000
 (US 2003/0144286, compound 52)	400

 (US 2003/0144286 compound 30)	440

6. The above-identified results are unexpected, as there is no expectation that the selection of structural features in the present compounds would improve the anti-ITK activity. The particular combination of structural features not taught or suggested by the prior art is that when the $\mathbf{R_4}$ moiety is



and the $\mathbf{R_3}$ group is : $-(CH_2)_n-$ **L-R**$_6$. Particularly when $\mathbf{R_6}$ is any cyclic group, then $\mathbf{R_6}$ is not directly attached to the benzimidazole nitrogen by virtue of **n** being a minimum of 1.

8. The above-identified results are commensurate in scope for the claimed subject matter, as there is no reason to expect that other compounds bearing the above-mentioned $\mathbf{R_4}$ and $\mathbf{R_3}$ groups, would not to exhibit similar activity.

7. The difference between the improved anti-ITK activity of the compounds of the present invention and that of the prior art are significant. Accordingly, the consumer would prefer the effective compound.

The undersigned petitioner declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 12/13/2005

Signature: Hidenori Takahashi

Hidenori Takahashi